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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,301	01/22/2001	Michal Eisenbach-Schwartz	EISENBACH-SCHWARTZ=18	8567

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/765,301	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,8,9,11-19,21-25,27-29,31-42 and 47-65* is/are pending in the application.

4a) Of the above claim(s) *2,9,15-19,21,23,27-29,32,38-42,50,52-55,58 and 62-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,11-14,22,24,25,31,33-37, 47-49, 51, 56-57, 59-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *2,8,9,11-19,21-25,27-29,31-42 and 46-65* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 22 September 2003 has been entered in full. Claims 1, 3-7, 10, 20, 30, 43-46 are cancelled and claims 2, 8-9, 11, 21-25, 27, 31-34 are amended. Claims 47-65 are added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Newly submitted claims 50, 52-55, 58, 62-65 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The claims are basically drawn to a method of causing activated T cells to accumulate at the site of neuronal degeneration by administering an effective amount of activated T cells that have been activated by Copolymer 1 or a Copolymer 1-related peptide. The newly submitted claims also recite that an individual is suffering from an injury that has caused primary neuronal damage. However, the elected invention recites the administration of Copolymer 1 (13 May 2002) and disease, specifically glaucoma (not injury), was elected as a species (13 May 2002).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 2, 9, 15-19, 21, 23, 27-29, 32, 38-42, 50, 52-55, 58 and 62-65 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's continued traversal of the Restriction requirement set forth in the communications of 23 January 2003 and 13 May 2002 appears moot since the restriction

requirement was made final in the Office Action of 30 July 2002. If Applicant wishes to pursue the matter further, a petition should be filed in accordance with 37 CFR 1.144.

Claims 8, 11-14, 22, 24-25, 31, 33-37, 47-49, 51, 56-57, and 59-61 are under consideration in the instant application as they read upon the elected invention of administering a Cop 1 or Cop 1 related polypeptide, as they read upon the elected species of Cop 1, disease, glaucoma, and a 4 different amino acid copolymer (alanine, glutamic acid, lysine, and tyrosine).

Withdrawn Objections and/or Rejections

1. The objection to claims 1, 8, 10, 22, 30-31, 33, and 43-44, and 46 for reciting non-elected species at pg 5 of the previous Office Action (21 April 2003) is *withdrawn* in view of the cancelled claims (22 September 2003).

2. The rejections to claims 22, 24-25, and 43-44 under 35 U.S.C. § 112, second paragraph, are *withdrawn* at pg 12-13 of the previous Office in view of the cancelled claims (22 September 2003). Please see section below on 35 U.S.C. § 112, second paragraph.

Specification

3. The objection to the disclosure regarding a suggested title change is maintained and held in abeyance until all other issues are resolved.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 47 and 51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47 and 55 of copending Application No. 09/314,161. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '161 application and the instant application recite a method of causing T cells activated against a NS-specific antigen (such as Cop 1) to accumulate at the site of neuronal degeneration in an individual in need. The recitation of reducing neuronal degeneration caused by neurodegenerative effects of disease, ameliorating the effects of an injury or disease that causes neuronal degeneration, and reducing neuronal degeneration in the central nervous system or peripheral nervous system in the preamble of the claims from the instant application and the '161 application is interpreted as an intended use and bears no accorded patentable weight. Therefore, the instant claims of a method of causing T cells activated against a NS-specific antigen (such as Cop 1) to accumulate at the site of neuronal degeneration is not patentably distinct over the co-pending claims in Application No. 09/314,161.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 8, 11-14, 25, 31, 33-37, 47, 49, 51, and 60-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 43-44, 46-49, 61-63, 65-69, 79, 81, and 88-89 of copending Application No. 09/765,644. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '644 application and the instant application recite a method of causing T cells activated by Copolymer 1 to accumulate at the site of neuronal degeneration in an individual in need. The recitation of reducing neuronal degeneration caused by neurodegenerative effects of disease, ameliorating the effects of an injury or disease that causes neuronal degeneration, and reducing neuronal degeneration in the central nervous system or peripheral nervous system in the preamble of the claims from the instant application and the '644 application is interpreted as an intended use and bears no accorded patentable weight. Therefore, the instant claims of a method of causing T cells activated by Copolymer 1 to accumulate at the site of neuronal degeneration is not patentably distinct over the co-pending claims in Application No. 09/765, 644.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 47 and 51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47 and 53 of copending Application No. 09/893,348. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '348 application and the instant application recite a method of causing T cells activated against a NS-specific antigen (such as Cop 1) to accumulate at the site of neuronal degeneration in an individual in need. The recitation of reducing neuronal degeneration caused by neurodegenerative effects of disease, ameliorating

the effects of an injury or disease that causes neuronal degeneration, and reducing neuronal degeneration in the central nervous system or peripheral nervous system in the preamble of the claims from the instant application and the '348 application is interpreted as an intended use and bears no accorded patentable weight. Therefore, the instant claims of a method of causing T cells activated against a NS-specific antigen (such as Cop 1) to accumulate at the site of neuronal degeneration is not patentably distinct over the co-pending claims in Application No. 09/893,348.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

8. Claims 8, 11-14, 22, 24-25, 31, 33-37, 47-49, 51, 56-57, and 59-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting secondary neuronal degeneration of ganglion cells caused or exacerbated by glutamate toxicity in the central nervous system (CNS) comprising administering to an individual with glaucoma an effective amount of Copolymer 1 (Cop 1) to inhibit secondary neuronal degeneration, does not reasonably provide enablement for a method of ameliorating the effects of disease or for a method of reducing neuronal degeneration caused by the neurodegenerative effects of disease which neuronal degeneration or secondary neuronal degeneration is caused or exacerbated by glutamate toxicity comprising causing activated T cells, which have been activated by Cop 1, to accumulate at the site of neuronal degeneration in the individual in need. The specification does not enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make and/or the invention commensurate in scope with these claims. The basis for this rejection is set forth at pg 5-11 of the previous Office Action (21 April 2003).

The claims also recite that the individual in need is suffering from a disease (glaucoma) that has neurodegenerative effects. The claims recite that Cop 1 is administered in a manner which promotes active immunization of the individual. Furthermore, the claims recite that Copolymer 1 is a random copolymer that cross-reacts functionally with MBP and competes with MBP on the MHC class II molecule in antigen presentation. The claims recite that the random copolymer comprises four different amino acids (alanine, glutamic acid, lysine, and tyrosine).

Applicant's arguments (22 September 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant indicates that Prof. Schwartz made a comprehensive presentation (interview of 26 June 2003) explaining the many successful experiments which have been undertaken in the laboratory to show the broad applicability of the technology involved with the present invention. Applicant argues that while much of the background and most the experiments dealt with T cells activated against Cop 1, some of it deals with other activated T cells. Applicant states that that which is now known about this technology allows one of ordinary skill in the art to understand that the predictions made in the present application would be expected to be accurate.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification teaches that mice are subcutaneously administered Cop-1 emulsified in complete Fruend's adjuvant (CFA) or phosphate-buffered saline (PBS) in CFA. The mice are then subjected to sever crush injury in the intraorbital portion of the optic nerve (pg 71).

Glutamate is injected into the right eye of the mouse and Fluorogold is injected into the superior colliculus of each hemisphere (pg 72). The specification discloses that immunization with Cop-1 results in a significant reduction in glutamate toxicity (pg 81, lines 1-2; Figure 8A-8C). The results also indicate that the protective efficacy of Cop-1 diminishes with the time between immunization and glutamate insult (pg 81, lines 12-13). However, the specification does not teach a reduction of neuronal degeneration caused by disease or caused or exacerbated by glutamate toxicity in the CNS of an individual comprising causing activated T cells, which have been activated by Cop-1, to accumulate at the site of neuronal degeneration. Undue experimentation would be required of the skilled artisan to determine which cell types in the central nervous system are inhibited from neuronal degeneration. There are a variety of neurons/CNS cells encompassed by the claimed methods, such as motor neurons, sensory neurons, glial cells, dopaminergic neurons, serotonergic neurons, oligodendrocytes, Schwann cells, and astrocytes. The specification only teaches that the number of surviving retinal ganglion cells in the Cop 1-immunized rats is significantly higher than in the PBS injected controls (pg 83, lines 1-4; Figure 11A-C). A large quantity of experimentation would be required by the skilled artisan to inhibit neuronal degeneration or reduce secondary neuronal degeneration of all possible CNS cells or neurons wherein the degeneration is caused or exacerbated by glutamate toxicity. The method of administering Cop 1 in the specification is not adequate guidance, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

Furthermore, there are also no methods or working examples in the specification to indicate that primary neuronal degeneration (or the primary damage) is reduced, as recited in the

claims. A large quantity of experimentation would be required of the skilled artisan to reduce primary neuronal degeneration of any cell type caused or exacerbated by glutamate toxicity. As discussed in the previous Office Action (21 April 2003), because of the lack of guidance provided by the specification as to how one can rescue dead or dying cells instantaneously affected, for example, by a head injury or neurodegenerative disease, there is no nexus that merely administering Cop 1 to an individual in need thereof can reasonably be extrapolated to successfully treat any human subject experiencing *"primary"* neuronal degeneration, as claimed, without undue experimentation to determine such. The examples in the specification of the instant application only indicate that administration of Cop 1 reduces *secondary* neuronal degeneration of ganglion cells caused or exacerbated by glutamate toxicity (see pg 83). Therefore, one skilled in the art would not expect an inhibition of secondary degeneration to also treat primary degeneration because the art indicates the primary "insult" or degeneration is irreversible and the processes involved in secondary degeneration are separate from those of the primary injury. Additionally, if secondary neuronal degeneration is inhibited and there is an ongoing insult to the neurons, one skilled in the art would not be able to predict that the primary degeneration would be inhibited in the same way that the secondary degeneration is.

Also, although the specification teaches that a large number of invading lymphocytes are observed in the vitreous 24 hours after glutamate injections (pg 91, lines 16-20), the skilled artisan would not be able to predict that those T lymphocytes are activated by Cop-1 since other antigens, such as MBP, MOG, and β-amyloid, may be present at the site of injury or disease in the central nervous system. There are also no methods or working examples in the instant application that indicate the invading T lymphocytes are activated by Cop-1.

Finally, undue experimentation would be required of the skilled artisan to determine the optimal dosage, duration, and route of administration of Cop 1 to reduce the neuronal degeneration caused by all possible diseases that involve glutamate toxicity, other than glaucoma. The scope of claims 47 and 51 encompasses diseases not expected to be commensurate with the elected species of glaucoma, such as Alzheimer's disease, Huntington's disease, prion diseases, etc. (pg 44, ¶ 2). The effects encompassed by these diseases are broad and may include for example, memory loss, cognitive deficits, behavioral changes, and dementia, which effects are not commensurate with glaucoma. The etiology and pathology of glaucoma is largely dissimilar from other diseases (particularly of the CNS) and the skilled artisan would not be able to predict that administration of Cop 1 would be beneficial for all possible diseases.

It is also noted that a broad, reasonable interpretation of the claims encompasses such diseases as Alzheimer's disease, Parkinson's disease, and Huntington's disease, among others, which have proven to be recalcitrant to treatment in the art (see for example, Halliday et al., Clin Exp Pharmacol Physiol 27: 1-8, 2000; Steece-Collier et al., Proc Natl Acad Sci USA 99(22): 13972-13974, 2002; Feigin et al. Curr Opin Neurol 15: 483-489, 2002). Therefore, undue experimentation would be required of the skilled artisan to inhibit neuronal degeneration, to treat disease or protect CNS cells in individuals by administration of Cop 1.

(ii) Applicant indicates that there are numerous references which relate to the present invention and reviews the results of several of them. Applicant argues that these papers establish for the record what Prof. Schwartz was able to explain at the interview of 26 June 2003.

Applicant submits that in light of all the experiments that have been done with respect to this invention, the full scope of the present would be expected to be operable. Applicant asserts that there is no reason to believe that undue experimentation would be involved in order to make and use the full scope of the present invention.

Applicant's arguments have been fully considered but are not found to be persuasive. Any references which the Applicant wishes for the Examiner to review and make of record should be supplied in the form of an Information Disclosure Statement pursuant to 37 C.F.R. § 1.98(a)(1) which requires a list of all patents, publications, or other information submitted for consideration by the Office. The list of references has been placed in the application file, but the information referred to therein has not been considered. Submission of the proper PTO-1449 form with copies of the references listed therein will be taken into due consideration by the Examiner. It is noted that the Examiner has previously considered a few of the references listed in the response of 27 August 2003 (for example, Moalem et al. (Nat Med 5(1): 49-55, 1999), Moalem et al. (J Neuroimmunol 106 : 189-197, 2000), Hauben et al. (Lancet 354 : 286-287, 2000), Hauben et al. (PNAS USA 98: 15173-15178, 2001, Hauben et al. J. Neurosci 20: 6421-6430, 2000). However, only the elected invention is being examined at this time. Until the elected invention is deemed allowable, the references are not pertinent. The references will be considered when allowable subject matter relevant to the elected invention is identified.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to determine which cells types are inhibited from neuronal degeneration or protected from glutamate toxicity, to inhibit primary neural degeneration of any cell, and to treat all possible diseases caused or exacerbated by glutamate

toxicity with Cop-1, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, unpredictability of the effects of treating diseases caused or exacerbated by glutamate toxicity with Cop 1, and the breadth of the claims which fail to recite limitations as to the type of neural degeneration caused by glutamate toxicity, the cells affected, and the disease to be treated, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

9. Claims 8, 11-14, 22, 24-25, 31, 33-37, 47-48, 51, 56-57, 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 8, 11-14, 22, 24-25, 31, 33-37, 47-48, 51, 56-57, 59 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the administration of Cop 1. The basis for this rejection is set forth at pg 12 of the previous Office Action (21 April 2003) and at pg 7 of the Office Action of 30 July 2002.

Applicant's arguments (22 September 2003) as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

At page 24 of the Response, Applicant argues that one does not look to the claims to find out how to practice the invention they define, but to the specification. Applicant also argues that no essential step is omitted, as the only essential step is causing the T cells to accumulate at the site of neuronal degeneration. Applicant argues that the administration of NS-specific activated

T cells is not essential step for causing T cells to accumulate at the site of injury. Applicant indicates that claim 50, which specifies that activated T cells are administered does not add a step to claim 47, but further defines the causing step.

Specifically, Applicant's arguments have been fully considered but are not found to be persuasive because it is inappropriate to read limitations in the specification into the claims. The claims must independently define the invention for which patent protection is sought. Therefore, the claims are still rejected as being indefinite because the claims do not recite a step which causes the NS-specific activated T cells to accumulate at the site of neuronal degeneration. It is noted to Applicant that the claims have been examined to the extent that they read upon the elected group of administration of Cop 1 (and not the administration of Cop 1 activated T cells).

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
01 March 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER